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ANALYSIS OF PROGNOSTIC FEATURES IN CHILDREN WITH THE HEMOLYTIC-UREMIC SYNDROME

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ABSTRACT

The purpose of this study has been to evaluate various factors influencing prognosis in children with hemolytic-uremic syndrome (HUS). Forty children with classical picture of HUS were seen in 1986-1991. Boys and girls were equally affected, aged from two months to ten years. In 35 patients (87.5%) there was a history of diarrhea which was bloody in 25. All were treated with peritoneal dialysis within the first 24 hours. Fresh frozen plasma (FFP) was transfused in the first two days for all except 11 patients for whom it was transfused in the third to fifth day of admission. Fifteen patients died (37.5%); of these, 12 (80%) had diarrhea for longer than 7 days, 11 (73%) had prominent neutrophilia, and 9 (60%) had significant neurological symptoms. Eleven of the fifteen patients had been transfused with FFP after the third day of hospitalization. Statistical analysis of data relating to mortality revealed the following regarding prognostic factors in HUS among children: mortality is higher in those with longer prodromal period ($p<0.001$), in those with bloody diarrhea ($p<0.025$), in patients with prominent neutrophilia ($p<0.001$), and in those who had delayed treatment with FFP ($p<0.001$). Prognosis was not affected by age, sex, or season of presentation.
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INTRODUCTION

The hemolytic uremic syndrome (HUS) is characterized by microangiopathic hemolytic anemia, thrombocytopenia and acute renal failure. It has been recognized as a major cause of acute renal failure in children. Endothelial injury, which results from localized activation of the coagulation system with subsequent deposition of fibrin-related antigens, is most pronounced in the kidneys. The purpose of this study has been to evaluate various factors influencing prognosis in children with the HUS.

PATIENTS AND METHODS

Medical records of seventy patients admitted from 1986 to 1991 with the diagnosis of HUS were reviewed. Thirty cases were excluded, either due to insufficient data or due to the fact that they had been cases of septicemia with renal failure. Forty cases fulfilling the accepted criteria for HUS have been included, twenty-one girls aged two months to ten years old and nineteen boys six months to four years old. All cases had hemolytic anemia with fragmented RBC's, thrombocytopenia, and elevated blood urea and creatinine levels. All had blood, urine, and stool cultures, and measurements of urine output. The interval between the first symptoms and hospitalization, interval between the time of hospitalization and treatment with dialysis, and administration of fresh frozen plasma (FFP) were calculated in all cases. If two or more cases occurred within the same or adjacent month, they were classified as "epidemic".[1] In statistical analysis, X^2 was used for categoric variables and t-test for continuous variables.

RESULTS

Of the forty cases, eight (20%) were under one year of age, four (10%) over five years, fourteen (35%) were 1-2 years of age, and fourteen (35%) were 2-5 years old. Distribution of age in both sexes was similar (Fig. 1), eight patients (20%) presented in late spring (June) and the next peak was in early autumn (Sept, Oct) (Fig. 2). History of diarrhea, which was bloody in 25, was obtained in 35 patients (87.5%). Twenty-four (60%) patients had neurological symptoms, such as localized or generalized convulsion, stupor, or coma. Twenty-nine (72.5%) presented with oliguria or anuria and eleven cases (27.5%) had elevated blood pressure. One child had an affected sibling, as well.

Fifteen (37.5%) of the patients died, of whom twelve (80%) had diarrhea, which was bloody in 50% ($p<0.025$). In these fifteen cases, twelve (80%) had diarrhea more than seven days prior to hospitalization ($p<0.001$). Eleven of the fifteen cases (73%) had prominent neutrophilia ($p<0.001$). All patients were treated with peritoneal dialysis within twenty-four hours but FFP was transfused after the third day of hospitalization in eleven cases who all died, while the rest of them received transfusion of FFP at an earlier time. Mortality in the group receiving early transfusion was noted to be 37.5% ($p<0.001$, compared to those with delayed transfusion), (Tables I-IV)

Fourteen (35%) patients had three months to two years follow-up, six of them (42%) had persistent renal impairment, four (21.4%) had neurological sequelae.

DISCUSSION

Gasser[2] provided the initial description of hemolytic-uremic syndrome with several discrete clinical variants. The mean age in all reports has been noted to be in infancy, as in our series in which 55% of cases occurred during the first two years of life. In outbreaks in Argentina, South Africa, and Southern California, distribution has been equal among females and males. In a few centers, females have been reported more often than males.[3,4] In our series, with the possibility of an outbreak in 1991 (Fig. 1), more females were involved (nine out of fourteen cases).

Preceding illness has been reported by Gianantonio[5] to be upper respiratory infection in 33%; in our series it has been noticed among 12.5% of cases. A report from Boston in 1988[6] showed that the duration of diarrhea and the occurrence of bloody diarrhea were not associated with the outcome; however, Trompeter's report from London in 1983[7] showed that a history of diarrhea at the onset with a short prodromal stage had a good outcome. In our series, diarrhea being bloody was relatively prognostically significant, while prodromal stage longer than seven days

Table I. Age Distribution of Patients With HUS

AGE(yr)	DIED	LIVING	TOTAL
<1	4	4	8
1-2	6	8	14
2-5	2	12	14
>5	3	1	4
TOTAL	15	25	40

Table II. Period of Diarrhea and Mortality in HUS

	≤7 DAY	>7 DAY	TOTAL
DIED	3	12	15
LIVING	17	3	20
TOTAL	20	15	35

P<0.001

Table III. Neutrophilia with FFP and Mortality in HUS

	NL PMN	↑ PMN	TOTAL
DIED	4	11	15
LIVING	21	4	25
TOTAL	25	15	40

P<0.001

Table IV. Treatment with FFP and Mortality in HUS

	Days 1-2	Days 3-5	TOTAL
DIED	4	11	15
LIVING	25	0	25
TOTAL	29	11	40

P<0.001

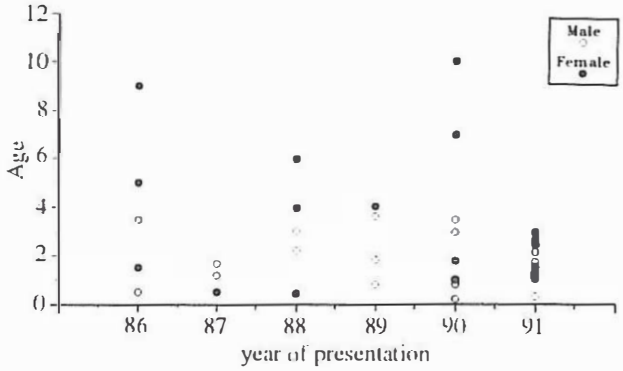

Fig. 1. Age of presentation of HUS acording to the year of study.

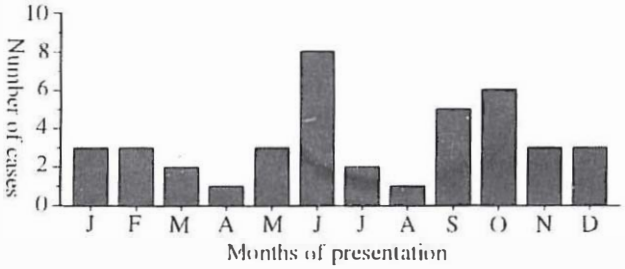

Fig. 2. Occurrence of HUS according to the month of the year.

was significant ($p<0.001$).

Central nervous system dysfunctions, observed in 60% of the cases, had no significant correlation with biochemical changes or hypertension and have most probably been due to cerebral edema. Bale's series[8] includes a patient who had CNS manifestations andconcomittant biochemical changes; autopsy in this case revealed cerebral edema.

The mortality rate in this study was 37.5%. Among 80% of the patients who died, the prodromal period was longer than seven days ($p<0.001$). All patients had peritoneal dialysis (PD), within the first twenty-four hours of admission. It has been shown that among patients treated by PD plus FFP transfusion, those transfused later than the first two days of admission had higher mortality.[9,10] Eleven of the fifteen dead cases were transfused in the 3rd-5th day of admission, showing delayed transfusion to be a significant contributor to mortality ($p<0.001$). It is concluded that in the HUS, mortality is higher among those with a longer prodromal period ($p<0.001$), in patients with prominent neutrophilia ($p<0.001$) and in those who received delayed treatment with FFP ($p<0.001$).

REFERENCES

1. Mc Lean MM, Jones CH, Sutherland DA: Haemolytic-uremic syndrome: report of an outbreak. Arch Dis Child 41: 76, 1966.
2. Gasser CE, Gautier E, Steck A, et al: Hamolytisch-uramische syndrome: bilaterale niereninden-nekrosen bei akuten erworbenen hamolytischen anamien. Schweiz Med Wochenschr 85: 905, 1955.
3. Riella MC, George CRP, Hickman RO, et al: Renal microangiopathy of the hemolytic-uremic syndrome in childhood. Nephron 17: 188, 1976.
4. Dolisager D, Tune B: The hemolytic-uremic syndrome: spectrum of severity and significance of prodrome. Am J Dis Child 132: 55, 1978.
5-Gianantonio CA, Vitacco M, Mendilaharzu F, et al: The hemolytic-uremic syndrome. Nephron 11: 174, 1973.
6. Havens PL, O'Rourke PP, Hahn J, et al: Laboratory and clinical variables to predict outcome in hemolytic-uremic syndrome. Am J Dis Child 142: 961, 1988.
7. Trompeter RS, Schwartz R, Chantler C, et al: Haemolytic-uremic syndrome: an analysis of prognostic features. Arch Dis Child 58: 101, 1983.
8. Bale JF Jr, Brasher C, Siegler RL: CNS manifestations of the hemolytic-uremic syndrome: relationship to metabolic alterations and prognosis. Am J Dis Child 134: 869, 1980.
9. Remuzzi G, Misiani R, Marchesi D, et al: Haemolytic-uremic syndrome: deficiency of plasma factor(s) regulating prostacycline activity? Lancet ii: 871, 1978.
10. Fong JSC, de Chadarenian JP, Kaplan BS: Hemolytic-uremic syndrome: current concepts and management. Pediatr Clin N Am 29: 825, 1982.